REMARKS

Claims 1-9 were presented at the time of filing. Claims 1-6 were cancelled and rewritten as new claims 10-13 in response to a Restriction Requirement and Amendment filed November 13, 2006. Claims 7-13 are currently pending in the application with claims 11-13 withdrawn from consideration as being directed to a non-elected invention.

Rejection under 35 U.S.C. § 102

The claims are rejected under 35 U.S.C. § 102(e) as being anticipated by Rapoport et al. (U.S 6,747,139.) According to the Office Action, Rapoport et al. disclose monoclonal antibodies against hTSH receptor which block binding of hTSH and autoantibodies to the receptor and Rapoport et al. also discloses the amino acid sequence of the hTSH receptor, which contains the FDSH sequence (amino acids 381-384.) From this the Office Action concludes that the antibody of Rapoport inherently has the ability to bind FDSH. Applicants disagree.

The claims are directed to monoclonal antibodies against the hTSH receptor. The claimed antibodies have two characteristics: 1) the antibodies have the ability to block binding of TSH and/or autoantibodies to the TSH receptor and 2) the antibodies bind to a specific epitope on the receptor having the amino acid sequence FDSH. In order for the cited reference to anticipate the claimed antibody, therefore, both characteristics of the antibody, as claimed, must be disclosed. Rapoport does not disclose either of the characteristics of the claimed antibody.

Anticipation under 35 U.S.C. §102

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros., Inc. v. Union Oil Co. of California, 814 F.2d628, 2 USPQ2d 1051, 1053 (Fed. Cir.

1987) The Federal Circuit uses two tests for inherent anticipation: "A reference includes an inherent characteristic if that characteristic is the 'natural result' flowing from the reference's explicitly explicated limitations." *Eli Lilly & Co. v. Barr Labs.*, 251 F.3d 955, 970 (Fed.Cir.2001). The Federal Circuit also recognizes a "necessarily present" test: "a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference." *SmithKline*, 403 F.3d at 1343 (citing *Continental Can Co. v. Monsanto* Co., 948 F.2d 1264, 1268 (Fed.Cir.1991)

In the present case, Rapoport et al. identify two intramolecular cleavage sites in the human TSH receptor and disclose compositions and methods for a convenient and economical source of recombinant TSH receptor. According to Rapoport et al., this identification "*...opens the way for future studies to answer many questions that have remained unanswered for a number of years. These questions include (a) the identification of the site(s) of binding (epitopes) of stimulatory and inhibitory anti-TSH receptor antibodies present in the sera of patients with autoimmune thyroid disease, and the relationship between these binding sites and that for TSH*" (col. 4 lines 19-26.) Rapoport et al. does not disclose the answers to these questions.

With respect to anti-TSHr antibodies, Rapoport et al. teaches (col. 15-19) various types of antibodies that can be obtained using known methodology when TSHr protein is used as antigen. These include polyclonal antibodies, monoclonal antibodies, antibody fragments, for example, Fab and $F(ab')_2$ (col. 15, lines 42-col. 16, line 9). Additionally, Rapoport et al. teaches use of anti-TSHr antibodies in various immunoassays (col. 16, line 17-26 and col. 18, line 41-60), and labeling of antibodies (col. 17, line 34- col. 18, line 33). Contrary to the Office Action's position, however, Rapoport et al. contains ***no*** disclosure of antibodies that block the binding of either TSH or stimulating autoantibodies to the receptor (blocking antibodies) nor does it identify any particular region of the receptor (a binding site, for example) that is particularly important for preparation of blocking antibodies.

Nor does Rapoport et al. disclose the use of peptides of TSHr to generate anti-peptide antibodies that bind to particular sites (for example, FDSH) on the receptor. It is likely that one skilled in the production of antibodies would employ a peptide that contains the FDSH sequence to ensure that an antibody directed to that epitope is produced since immunization with the intact TSHr as antigen will give rise to antibodies to a multitude of epitopes. This is not sufficient to establish inherency.

Inherent anticipation requires that the "missing characteristic is necessarily present, or inherent, in the single anticipating reference." *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1377 (Fed.Cir.2003) To support an anticipation rejection based on inherency, an examiner must provide factual and technical grounds establishing that the inherent feature necessarily flows from the teachings of the prior art. See Ex parte Levy, 17 USPQ 2d 1461, 1461 (BPAI1990); see also In re Oelrich 666 F.2d 578, 581, 212 USPQ 323 326 (CCPA1981) holding that inherency must flow as a necessary conclusion from the prior art, not simply a possible one.

The inherency analysis enunciated in the present Office Action goes astray because it assumes what Rapaport et al. neither disclosed nor rendered inherent: an antibody that 1) blocks binding of TSH or to the receptor or 2) specifically recognizes/binds the FDSH epitope. In suggesting that the claimed antibodies are inherently anticipated by Rapaport et al., the Office Action incorrectly assumes that an antibody specific for the FDSH epitope would necessarily flow from immunization of an animal with TSHr protein. Immunization with intact TSH receptor will give rise to antibodies of many different specificities, not just to a single epitope on the receptor molecule and not necessarily to an antibody that will block binding of TSH or autoantibodies to the receptor.

Withdrawal of the rejection under 35 U.S.C. §102 is respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 7-8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rapaport et al. (U.S. Patent No. 6,747,139), in view of Vanderbark et al. (U.S. Patent No. 5,614,192). According to the Office Action, it would have been obvious to one of skill in the art to humanize the antibodies of Rapoport by using the method of Vandenbark.

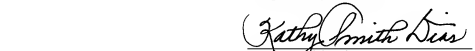
As discussed above, Rapoport et al. does not teach an anti-hTSH receptor antibody that blocks binding of TSH and autoantibodies to the receptor and additionally binds to the FDSH (amino acids 381-384) amino acid sequence of the hTSH receptor.

Vandenbark discloses T-cell receptor peptides and antibodies directed thereto. The teachings of Vandenbark do not compensate for the deficiencies in the teachings of Rapoport et al., because, like Rapoport et al., Vandenbark fails to teach the significance of the FDSH sequence of the hTSH receptor and an antibody directed thereto. In the absence of such teaching, there is no motivation to make the claimed antibody, let alone humanize it. Accordingly, the combination of teachings of Rapoport and Vandenbark do not result in Applicants' claimed antibodies.

In view of the above arguments, withdrawal of the rejection under 35 U.S.C. §103 is respectfully requested.

It is respectfully submitted that the above-identified application is now in a condition for allowance and favorable reconsideration and prompt allowance of these claims are respectfully requested. Should the Examiner believe that anything further is desirable in order to place the application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,



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Dated: August 22, 2008

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